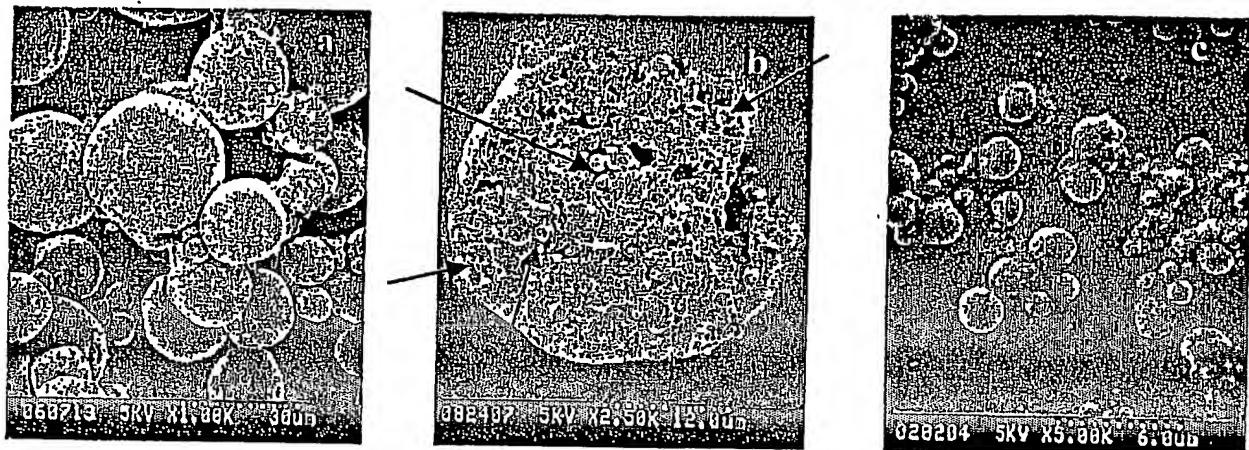


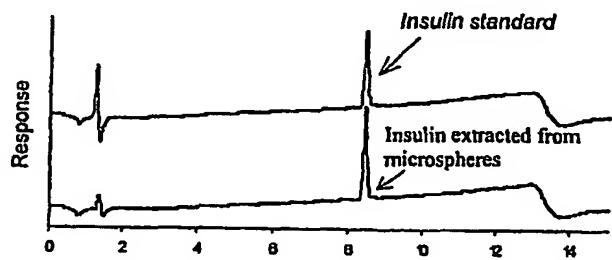
1/8

**Figure 1.** SEM micrographs of insulin-loaded AcHES-PLGA composite microspheres (a), interior structure of a fractured microsphere (b, arrows point to embedded AcHES microparticles) and freeze dried AcHES hydrogel microparticles (c).



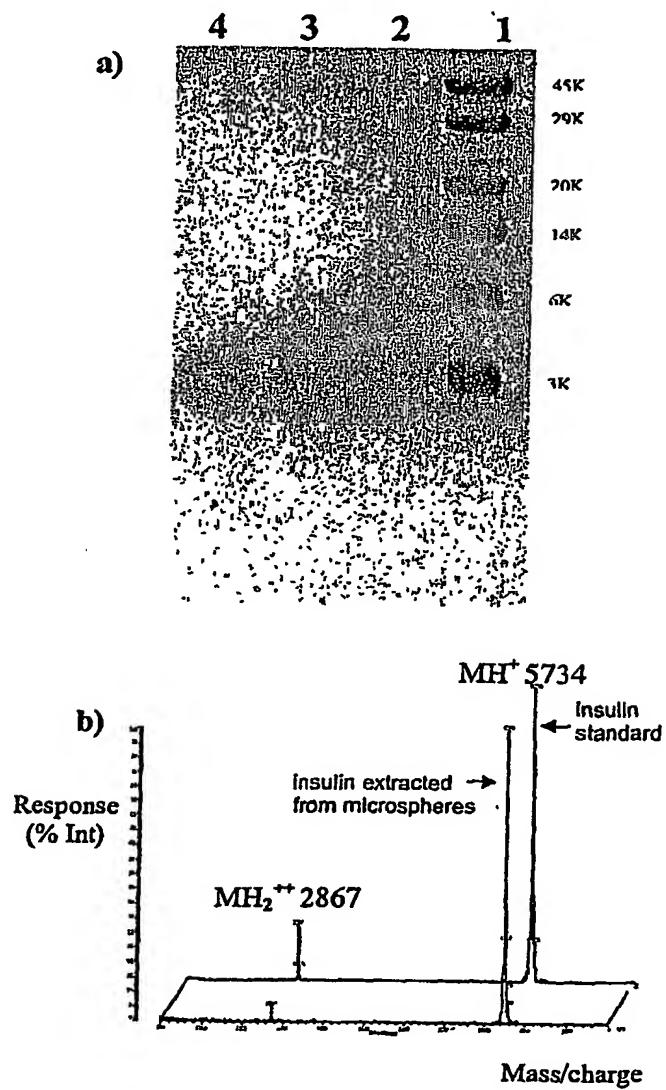
2/8

Figure 2. HPLC chromatogram of insulin sample isolated from composite microspheres by ACN extraction and intact insulin standard.



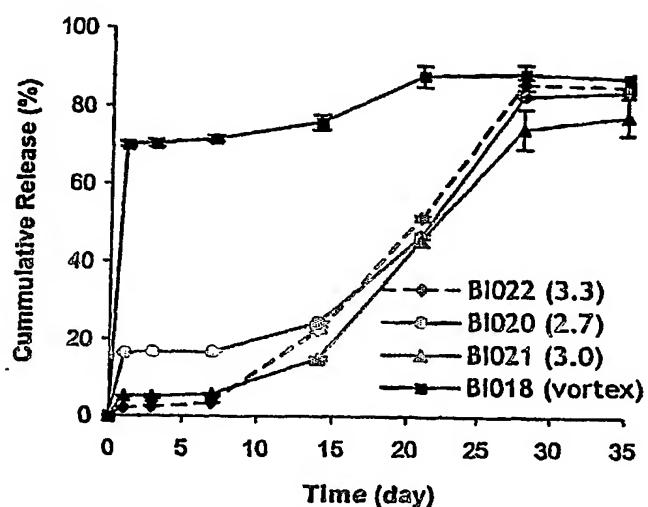
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Figure 3. Characterization of insulin integrity in the composite microspheres (a) SDS-PAGE with DTT. Lane 1, Molecular weight marker; Lane 2, Bovine insulin standard; Lane 3, insulin sample from BI021 and lane 4, insulin sample from BI022. (b) MALDI-TOF MS of insulin extracted from composite in comparison to intact standard.



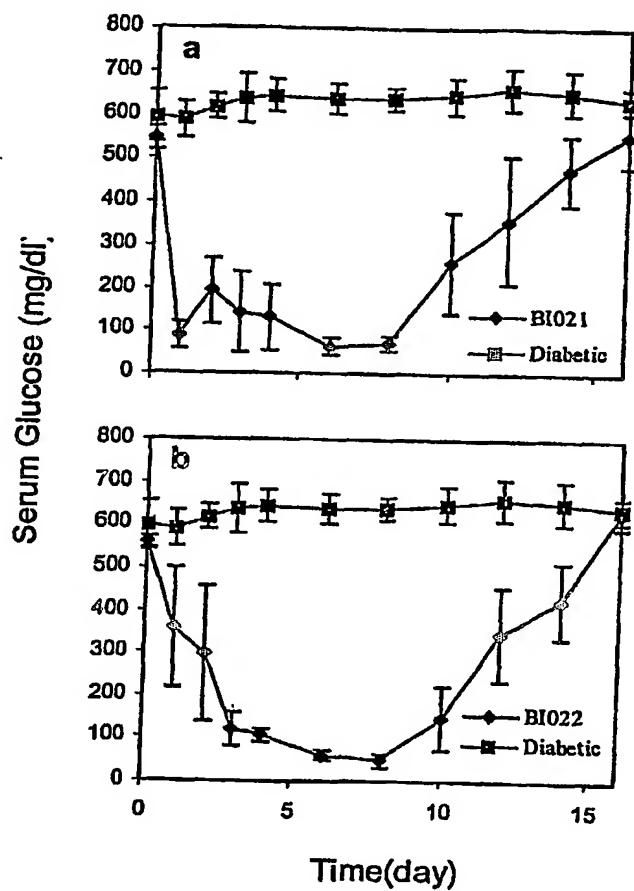
4/8

Figure 4. In vitro release of insulin from composite microspheres in glycine buffer at 37°C. Sonication levels are indicated in ( ).



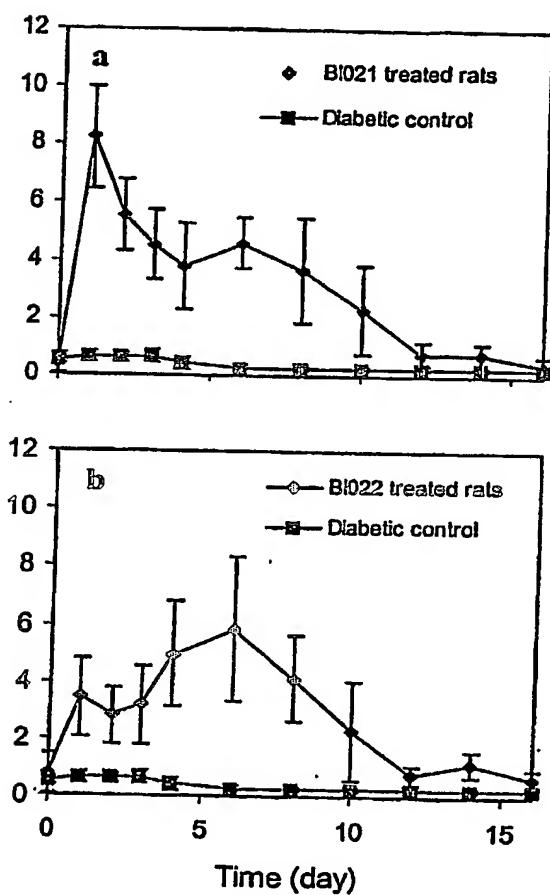
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Figure 5. Serum glucose suppression in diabetic rats treated with insulin loaded composite microsphere batches BI021 (a) and BI022 (b).



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Figure 6. Serum Insulin level of (a) BI021 and (b) BI022 treated diabetic rats.



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Figure 7. Blood glucose suppression of multiple dosing treatment of insulin loaded composite microspheres ( $n=8$ , Dose 80 IU/rat).

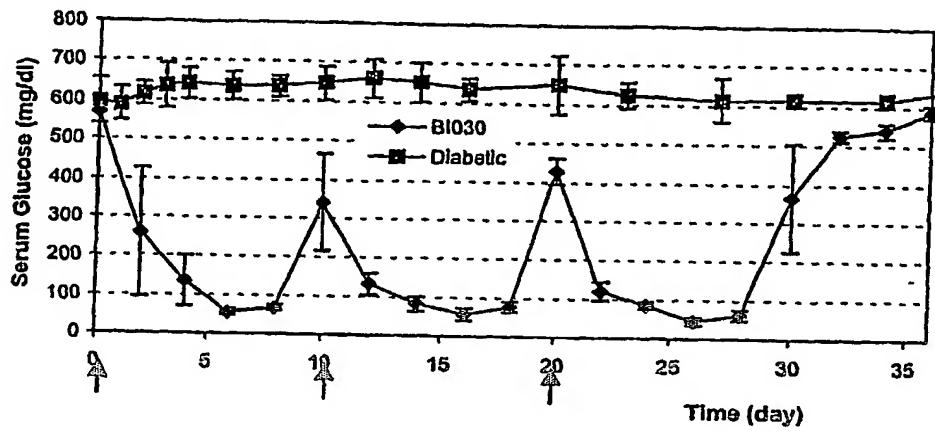


Figure 8. Serum insulin level of multiple dosing treatment of insulin loaded composite microspheres ( $n=8$ , Dose 80 IU/rat).

